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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/325,019	06/03/1999	PAUL E. YOUNG	PF467	2297

22195 7590 12/24/2002

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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/24/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 4/5/02

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 24,34-46,51,53,55-148 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 24,34-46,51,55-66# is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 17
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1998-421-632/40208

Part III: Detailed Office Action

Restriction Requirement:

The elected invention remains nucleic acids which encode SEQ ID NO: 2, residues 1-335. Thus, claims 24, 34-46, 51 and 55-66, are under consideration. Newly introduced claims 106-148 are withdrawn from prosecution as being drawn to a non-elected invention.

Formal Matters:

The new title of the invention is acknowledged.

The rejections under 35 U.S.C. § 112, second paragraph, are withdrawn in view of applicants arguments. However, should applicants overcome the rejection under 35 U.S.C. § 101 and 112, first paragraph, a rejection of the claims would still be maintained under 35 U.S.C. § 112, first paragraph, on the basis that enablement would not be commensurate in scope with the claims, in view of applicants' broad assertions of the claimed breadth.

In the previous Office Action, the Examiner stated that references AE-AI were not considered as they are merely sequences with no explanation of relevance or alignment with the disclosed sequences, such that relevancy to the claimed invention cannot be assessed. Applicants have traversed this, and have cited the same references again. Applicants traversal has been considered, and found persuasive. The sequences have been considered. However, because there is no statement of relevancy or alignment to the claimed subject matter, the relationship of those sequences to what is claimed cannot be determined.

Objections and Rejections under 35 U.S.C. §§101 and 112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 24, 25, 34-46, 51 and 55-66 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for reasons cited in the previous Office Action, paper number 14 mailed 11/7/01, at page(s) 5-8. Applicant's traversal, in paper number 16, filed 4/9/02, has been fully considered but is not deemed persuasive:

At page 15, applicants contend that those of skill in the art routinely rely on homology as predictive of protein function. This argument has been fully considered but is not deemed persuasive because while the art certainly appreciates that conserved structure may be indicative of function, the standard in the art is to *test* molecules to confirm activity. As evidenced by references cited in the previous Office Action, there are numerous instances in the prior art wherein closely related peptides have distinct, and sometimes even opposite, biological activities. Applicants argue that the Examiner has "presented no evidence directed to CTGF or HBGF, the most closely related proteins. This argument has been fully considered but is not deemed persuasive because the Examiner cannot manufacture evidence; she is constrained to citing what can be found in the prior art. The *prima facie* case has been made that CTGF-4 is only 45% identical to CTGF, and, based upon a rough calculation, about 55% identical to the region corresponding to HBGF, and that one of skill in the art would not consider this level of identity to be predictive of function. Applicants have provided neither fact nor evidence to overcome this *prima facie* finding. The issue is not that the asserted utilities are *inconsistent* with those of other proteins, but rather that the utilities of such other proteins would not be accepted by one of ordinary skill in the art as being predictive of the disclosed "CTGF-4".

Continuing at page 16, applicants cite post-filing date publications that disclose that WISP-1, which is the same as CTGF-4, is overexpressed in rat kidney fibroblast cells, induced morphological transformation, accelerated cell growth, and enhanced saturation density, induced tumor formation in nude mice, was found in elevated levels in primary breast cancers, etc. This argument has been fully considered but is not deemed persuasive because *none* of the activities reported in the post-

filing date art pertains to any specifically disclosed utility. First of all, finding that a gene is overexpressed in a certain cancer type is not sufficient to establish diagnostic utility:

The determination of a cancer marker must be based on studying results from a considerable number of patients, and statistical analysis. For instance, the Guidelines for Marker Development by the National Cancer Institute (NCI) clearly indicate the data required to proceed, and the considerations for preliminary identification of a potentially useful marker in the initial step. Some of the considerations in the Guidelines are:

> "Step 1: ... Can a patient *population* be defined for which this marker may have utility? What is an expected range for the prevalence of this marker in population of potential interest? .... The number of specimens that should be assessed at this stage will vary depending on the question asked or the intended use of the marker. If *prevalence is being assessed*, then >20 specimens should be examined so that a marker present in 5% of cases would have a reasonable chance of being detected in the set of specimens. The numbers to be assessed for other questions will depend on the statistical design, the difference that would be meaningful to detect. .... Estimate prevalence of the marker on an *expanded* collection of targeted specimens. Step 5: ... The intended use should be more clearly defined and careful *statistical* designs applied to studies that usually have to include *large number of cases*."

For obvious reasons, none of the critical questions or considerations for the determination of a cancer marker above are sufficiently answered or met by the cited publications. Further, and most importantly, the post-filing date art cannot substitute for the lack of disclosure of a specific, substantial and credible utility. Applicants assertions based upon the post-filing date are drawn to very specific uses, which were not specifically disclosed in the specification as originally filed. It remains that the invention was incomplete as disclosed, and applicants cannot rely on post-filing date art to establish completion of the invention.

At pages 16-18 applicants once again review the post filing date art, concluding that "the present invention is useful for the purposes asserted in the specification, namely modulating mitogenic activity of fibroblasts and tumors." This argument has been fully considered but is not deemed persuasive because applicants have failed to point out, and the

Examiner cannot locate in the specification as originally filed that the present invention is useful for "modulating mitogenic activity of fibroblasts and tumors". Further, it is not clear *how* applicants conclude such based upon the post-filing date art: Xie et al. merely conclude that WISP-1 "*might* serve as a valuable tool for monitoring tumor status of breast cancer patients" which is both speculative and not supported by the specification as originally filed, Su et al. study the role of WISP-1 in apoptosis, which is not correlated with any disclosed utility, Desnoyers et al. disclose that WISP-1 binding was restricted to the stroma of colon tumors and to cells with a fibroblastic phenotype, which is not correlated with any disclosed utility, Xu et al. identifies WISP-1 as an oncogene, but not as a cancer diagnostic or other utility that was disclosed in the specification as originally filed,

Even *if* WISP-1 were found to be a cancer diagnostic, the specification as originally filed would not support the breadth of the claims. Cancer is not a single disease. Rather, there are many different types of cancer, with different etiologies, different characteristics, cell types, etc. While WISP-1 *may* be shown, after the filing date of this application, to have utility as a cancer diagnostic, it would be for a particular type or types of cancer, and not for cancer generically. The discovery of what types of cancer it would be diagnostic for is considered by the Examiner to be part of the invention itself, and not to be supported by the generic disclosure of "cancer diagnostic" as found in the specification as originally filed.

At page 17, applicants argue that "utility can exist for therapeutic inventions "despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition." The Examiner takes no issue with the guidance in the MPEP. However, there is no disclosed, specific therapeutic regimen or pharmaceutical use for the claimed nucleic acids. It remains that the specification merely conjectures as to possible uses, many of which are non-specific, and provides no credible support for those that are. When applicants state that all heat is needed is a reasonable correlation between the biological activity and the asserted utility, they fail to point out what biological activity and utility they

refer to. It remains that the Examiner cannot locate in the specification as originally filed that the present invention is useful for "modulating mitogenic activity of fibroblasts and tumors". Further, it is not clear *how* applicants conclude such based upon the post-filing date art, for reasons cited above. Applicants arguments do not clearly relate to any specific disclosed utility. Thus, it remains that there was no specific, substantial, and credible utility asserted for the claimed nucleic acids, nor are any of the specific asserted utilities sufficiently supported by the subsequent art so as to confer utility to the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 25, 34-46, 51 and 55-66 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Advisory Information:

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

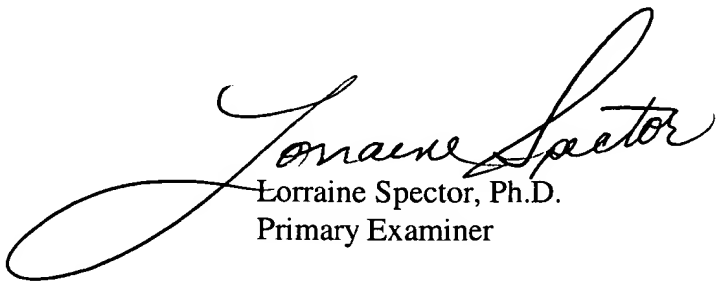
calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Spector via telephone number 703-746-5228. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.



Lorraine Spector, Ph.D.
Primary Examiner

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